

**BONE MINERAL DENSITY IN PATIENT
ADMITTED TO HOSPITAL RAJA
PEREMPUAN ZAINAB II WITH PROXIMAL
FEMUR FRACTURE**

By

Dr. Noor Hidayah Abdullah@Abd Wahab

**Dissertation submitted in Partial Fulfillment of the
Requirements for the Degree of Master of Medicine
(Orthopaedics)**



2016

ACKNOWLEDGEMENT

To

My Loving Husband and Daughter

Mr Amir bin Zainal Rasid & Nur Iman binti Amir

In the name of Allah, Most Gracious, Most Merciful. Along the journey of my studies, I have been encouraged, supported and inspired by many people. Here, I would like to take this opportunity to express my thanks to several people for their contribution to the development and completion of this dissertation.

First of all, my deepest acknowledgement goes to my dissertation supervisor, Professor Dr Abdul Nawfar Sadagatullah, who has generally offered his time, expertise, wisdom, and continuous encouragement in guiding me step by step through the whole research process.

My sincere thanks goes to my co-supervisor, Mr Muhd Anwar Hau Abdullah for his invaluable opinion which helped me tremendously in obtaining the data for this study.

My special thanks to Puan Syazwani for helping me overcoming the statistical obstacle and producing the final results of this study.

Finally, my warmest thanks to my dear husband, for his continued and unfailing love, support and understanding underpins my persistence in the graduate career and makes the completion of this dissertation possible.

TABLE OF CONTENTS

TABLE OF CONTENTS

ACKNOWLEDGEMENT	i
TABLE OF CONTENTS	iv
LIST OF FIGURES	vii
LIST OF TABLES	x
ABSTRACT	xi
ABSTRAK	xii
ABSTRACT	xiv
INTRODUCTION	1
1. INTRODUCTION	2
1.1 Rationale of the study	5
1.2 Research Questions	5
LITERATURE REVIEW	6
2. LITERATURE REVIEW	7
2.1 Introduction	7
2.2 Definition osteoporosis	7
2.3 Classification and clinical presentation of osteoporosis	9
2.4 Risk factor for osteoporosis	13
2.5 Diagnosis	16
2.6 Prevention of fracture	29
2.7 Proximal Femur Fracture	30
2.8 Definition Proximal Femur Fracture	31
2.9 Aetiology proximal femur fracture	33
2.10 Diagnosis proximal femur fracture	35
2.11 Surgical option proximal femur fracture	37
OBJECTIVES	41

3. OBJECTIVES	42
3.1 Main Objective	42
3.2 Spesific Objectives	42
METHODOLOGY	43
4. METHODOLOGY	44
4.1 Study design	44
4.2 Sample size	44
4.3 Sampling method	45
4.4 Inclusion and exclusion criteria	45
4.6 Statistical analysis.....	50
RESULTS	51
5. RESULTS.....	52
DISCUSSION	74
6. DISCUSSION	75
CONCLUSION.....	80
7. CONCLUSION	81
7.1 Limitation	82
7.2 Suggestion	83
REFERENCES	84
8. REFERENCES.....	85
APPENDIX.....	90
9. APPENDIX	91

LIST OF FIGURES

Figure 2.1: Bone Loss during adult life (Riggs BL et al 1986)	9
Figure 2.2: Changes in bone mass in aging men and women showing pattern of bone loss. (I) Peak bone mass, (II) rapid phase of bone loss in women around menopause, (III) is age related bone loss, similar in men and women (Riggs BL et al 2001).	12
Figure 2.3: Osteoporosis Self-assessment Tool for Asia (OSTA) and treatments.....	15
Figure 2.4: Normal trabecular pattern of proximal femur (taken from Manmohan Singh et al 1970)	19
Figure 2.5: Singh Index (Gaphics are from orthoedicnotes.blogspot.com)	20
Figure 2.6: Scan printout of the spine DXA examination with interpretation in term of T and Z-scores (Kwang J Chun et al 2011)	25
Figure 2.7: Scan printout of the hip DXA examination with interpretation in term of T and Z-scores (Kwang J Chun et al 2011)	26
Figure 2.8: KPH hip protector (Image is from hiprotector.com)	29
Figure 2.9: Classification of proximal femur fracture (Martyn J. Parker 2010)	32
Figure 2.10: Region anatomy of proximal femur (Image from orthoassociates.com).....	33
Figure 2.11: Possible causes of proximal femur fracture (Martyn J. Parker 2010) .	34
Figure 2.12: Undisplaced intracapsular fracture.	36
Figure 2.13: Intracapsular fracture treated by fixation with three parallel screws (Martyn J. Parker 2010)	37
Figure 2.14: A cemented hemiarthroplasty used to treat a displaced intracapsular fracture in elderly (Martyn J. Parker 2010)	38
Figure 2.15: Sliding hip screw fixation of a trochanteric fracture (Martyn J. Parker 2010)	39
Figure 2.16: An intramedullary nail has been used to fix a subtrochanteric fracture; the fracture has healed (Martyn J. Parker 2010)	40
Figure 4.1: Hologic Discovery W DXA machine	47
Figure 4.2: Position for lumbar BMD measurement	49
Figure 4.3: Position for hip BMD measurement	49
Figure 5:1: Distribution of elderly patients admitted for proximal femur fracture in HRPZ II from May 2012 till April 2014	52

Figure 5.2: Age distribution of patients admitted for proximal femur fracture in HRPZ II from May 2012 till April 2014	53
Figure 5.3: Gender distribution of patients admitted for proximal femur fracture from May 2012 till April 2014	54
Figure 5.4: Ethnic distribution of patients admitted for proximal femur fracture in HRPZ II from May 2012 till April 2014	54
Figure 5.5: Age distribution of patients admitted for fracture in HRPZII participating in the study	56
Figure 5.6: Age distribution between genders among participants in the study	56
Figure 5.7: Gender distribution of patients admitted for proximal femur fracture in HRPZII participating in the study	57
Figure 5.8: Distribution duration of menopause among female subjects participating in the study	57
Figure 5.9: Ethnic distribution of patients admitted for proximal femur fracture in HRPZII participating in this study	58
Figure 5.10: Smoking status of patients admitted for proximal femur fracture in HRPZII participating in this study	59
Figure 5.11: Milk drinker status of patients admitted for proximal femur fracture in HRPZII participating in this study	59
Figure 5.12: Income range (in RM) of patients admitted for proximal femur fracture in HRPZII participating in this study	60
Figure 5.13: Distribution of number of children among female subjects participating in this study	60
Figure 5.14: BMI categories of patients admitted for proximal femur fracture in HRPZII participating in this study	61
Figure 5.15: Distribution of T-score of Total hip among subjects participating in this study	62
Figure 5.16: Distribution of T-score of Spine among subjects participating in this study	62
Figure 5.17: Distribution of T-score of Neck of hip among subjects participating in this study	63
Figure 5.18: Total Hip bone density distribution among patients admitted for proximal femur fracture in HRPZII participating in this study	64

Figure 5.19: Spine bone density distribution among patients admitted for proximal femur fracture in HRPZII participating in this study	65
Figure 5.20: Neck of hip bone density distribution among patients admitted for proximal femur fracture in HRPZII participating in this study	65
Figure 5.21: Total Hip bone density group among subjects group participating in this study	66
Figure 5.22: Spine bone density group among subjects group participating in this study	66
Figure 5.23: Neck of hip bone density group among subjects group participating in this study	67
Figure 5.24: Mean T-Score value for total hip BMD in osteoporosis and non-osteoporosis	68
Figure 5.25: Mean T-Score value of spine BMD in osteoporosis and non-osteoporosis	68
Figure 5.26: Mean T-Score value for neck of hip BMD in osteoporosis and non-osteoporosis	69
Figure 5.27: Mean T-score for total hip bone density between genders	69
Figure 5.28: Mean T-score spine bone density between genders	70
Figure 5.29: Mean T-score neck of hip bone density between genders	70

LIST OF TABLES

Table 2.1: The World Health Organization (WHO) working group classification of osteoporosis.....	9
Table 2.2: Secondary Osteoporosis.....	10
Table 2.3: Characteristics of osteoporosis type 1 and type 2 (Riggs BL et al 2001).	11
Table 2.4: Risk Factors (From National Osteoporosis Foundation 1999: Physician's guide to prevention and treatment of Osteoporosis)	15
Table 2.5: Risk stratification	16
Table 2.6: Singh index description (from Manmohan Singh et al 1970).....	20
Table 2.7: Indications for BMD Measurement (Malaysian CPG 2006)	28
Table 2.8: Risk factors for proximal femur fracture (Martyn J. Parker 2010).....	34
Table 5.1: Distribution of bio-demographic profiles of patients with proximal femur fracture participating in the study	55
Table 5.2: Descriptive data of bone density of patients admitted for proximal femur fracture in HRPZII participating in this study	61
Table 5.3: Bone density distribution among patients admitted for fracture proximal femur in HRPZII participating in this study	63
Table 5.4: Mean of T-score for osteoporosis and non-osteoporosis comparison	67
Table 5.5: Mean of T-score for male and female comparison	68
Table 5.6: Association between bio-demographic and total hip neck bone density among patients participating in this study	71
Table 5.7: Association between bio-demographic and spine bone density among patients participating in this study	72
Table 5.8: Association between bio-demographic and Neck of Hip Bone density among patients participating in this study	73

ABSTRACT

ABSTRAK

Penyakit Osteoporosis telah pun biasa diperkatakan dan ia telah menyebabkan kepada insiden kepatahan tulang sebanyak 8.9 juta kes setiap tahun. Kebanyakan kajian kepatahan tulang femur atas mengatakan osteoporosis adalah penyebab utama walaupun tiada satu kajian pun mengatakan nilai kepadatan tulang yang dapat mengelakkan daripada kepatahan sedemikian berlaku.

Objektif

Kajian ini adalah Analisis Keratan rentas untuk menentukan nilai kepadatan tulang pesakit-pesakit berumur yang dimasukkan ke hospital disebabkan kepatahan tulang femur atas sepertimana yang ditentukan oleh mesin Imbasan DXA dan juga menentukan bio-demography pesakit-pesakit tersebut.

Metodologi

Nilai kepadatan tulang seramai 15 orang pesakit yang mengalami kepatahan tulang femur atas ditentukan menggunakan mesin Imbasan DXA. Nilai skor T akan dikaji secara lebih terperinci untuk mengetahui perkaitan dengan osteoporosis dikalangan pesakit di atas.

Keputusan

Nilai purata umur di kalangan pesakit adalah 70 tahun, dan 80% daripada mereka adalah berbangsa melayu. 60% daripada mereka tidak mengambil pemakanan berasaskan susu, dan 80% datang dari kalangan berpendapatan rendah. Hanya 33% adalah perokok. Kepadatan tulang neck hip di kalangan pesakit menunjukkan bacaan median terendah -1.70 dan julat interkuartil adalah 1.10. Seterusnya, bacaan

kepadatan tulang diikuti oleh hip keseluruhan dan spine masing-masing dengan bacaan median -1.60 dan -1.40. Sebahagian besar pesakit yang terlibat dalam kajian ini mempunyai kepadatan mineral tulang kumpulan osteopenic. Peratusan osteopenic tertinggi adalah neck hip dengan bacaan 66.7%. Diikuti dengan hip keseluruhan dan spine masing-masing dengan nilai bacaan 60.0% dan 33.3%. Peratusan pasakit di bawah kumpulan osteoporosis masing-masing untuk hip keseluruhan, spine dan neck hip adalah 6.7%, 33.3% and 20%. 5 (33.3%) pesakit mempunyai nilai BMD hip keseluruhan sebagai normal, 5 (33.3%) pesakit untuk spine dan 2 (20%) pesakit untuk neck hip. Dari keseluruhan 15 pesakit, hanya seorang pesakit mempunyai nilai ketiga-tiga tempat kepadatan tulang sebagai osteoporosis. Analisis ketepatan Fisher menunjukkan tiada signifikan perkaitan antara bio-demografik dan nilai kepadatan tulang di kesemua kawasan yang telah di nilai.

Kesimpulan

Kajian menunjukkan tiada signifikan perkaitan antara bio-demografik dan nilai kepadatan tulang di kesemua kawasan yang telah di nilai. Sebahagian besar pesakit yang terlibat dalam kajian ini mempunyai kepadatan mineral tulang kumpulan osteopenic. Peratusan osteopenic tertinggi adalah neck hip dengan bacaan 66.7%, diikuti dengan hip keseluruhan dan spine masing-masing dengan nilai bacaan 60.0% dan 33.3%.

Kata Kunci: Nilai kepadatan tulang, Imbasan DXA, osteoporosis, kepatahan tulang femur atas

ABSTRACT

Osteoporosis has been recognized as an established and well-defined disease that affects more than 8.9 million fractures annually worldwide. Most studies of fracture involving the proximal femur claim that generalized osteoporosis is the major etiological factor, although none has established a densitometric fracture threshold above which such fractures would not occur.

Objectives

This is a cross sectional analytical study with aims to identify the bone mineral density of elderly patients admitted for fracture proximal femur in an institution as assessed by Dual Energy X-Ray Absorptiometry (DXA) scan as well as to determine the biodemographics of the said profiles.

Methodology

Bone mineral density of 15 patients admitted for proximal femur fractures were evaluated using DXA scan. The T-score was further evaluated to see the significance of osteoporosis in these subjects.

Results

The mean age of the subject was 70 years old, and 80% were malays. 60% of them were non-milk consumer, and 80% were categorized under low socioeconomic group. Only 33% were a smoker. Bone density of neck of hip among the patients had the lowest median with -1.70 and interquartile range of 1.10. Then, it was followed by bone density for total hip and spine with median value of -1.60 and -1.40 respectively. Majority of the patients who involved in this study had their bone

mineral density value as osteopenia. The highest osteopenia percentage was for the neck of hip, 66.7 %. Then it was followed by total hip and spine, 60% and 33.3 % respectively. The percentage of patients with osteoporotic group of BMD for total hip, spine and neck of hip were 6.7%, 33.3% and 20% respectively. 5 (33.3%) patients had their BMD total hip as normal, 5 (33.3%) patients for spine and 2 (20%) patient for neck of hip. Out of 15 subjects, only 1 who had all three BMD value of total hip, spine and neck of hip as osteoporosis. Fisher's Exact test analysis found that there were no significant association between studied bio-demographic and bone mineral density at all measured sites.

Conclusion

This study found that there were no significant association between studied bio-demographic and bone mineral density at all measured sites. Majority of the patients who involved in this study had their bone mineral density value as osteopenia. The highest osteopenia percentage was for the neck of hip, 66.7 %, followed by total hip and spine, 60 and 33.3 % respectively.

Keywords: Bone mineral density, DXA scan, osteoporosis, proximal femur fracture

INTRODUCTION

1. INTRODUCTION

Osteoporosis is a worldwide problem with significant economic and social impact. Osteoporosis related fracture has been recognized as a major health problem, particularly in elderly. Hip fractures are associated with high morbidity and mortality rate up to 20% in the first year. Majority of those who survive are disabled and only 25% will resume normal activities. In 1997, the incidence of hip fracture in Malaysia among individuals above 50 years old was 90 per 100 000 cases. The direct hospitalization cost for hip fracture in 1997 in Malaysia was estimated at RM 22 million. This was a gross underestimate of the total economic burden, as it does not take into account the costs involved in rehabilitation and long term nursing care of the involved patients (Clayer and Bauze 1989). Affected patients may develop associated complications such as pressure ulcers, pneumonia, urinary tract complications and severe depression. Half of those who were ambulatory before the fractures are unable to walk without assistance subsequently and one-quarter require long-term domiciliary care (Phillips et al 1988).

Because bone loss occurs insidiously and is initially asymptomatic, osteoporosis is often only diagnosed after the first clinical fracture has occurred (Vestergaard et al 2005). Consequently, the aim of therapy is usually prevention of further fractures. Early assessment of an individual's risk of osteoporosis is therefore important to prevent the first fracture. Providing an easily available and cost effective screening tool for initiation of treatment and treatment monitoring are important in preventing the devastating outcome of osteoporosis.

National and international guidelines have been implemented to address the challenge of screening for osteoporosis in an evidence-based and cost-effective manner. Several risk factors, such as age, low body-mass index, previous fragility

fractures, a family history of fractures, the use of glucocorticoids, and active cigarette smoking have to be taken into account (Kanis 2002). The measurement of BMD by DXA is a valid method to diagnose osteoporosis and to predict the risk of fracture (Cummings et al 2002). New decision-making methods, such as the fracture-risk assessment tool (FRAX), have integrated clinical risk factors with DXA-based BMD to predict an individual's 10-year risk of sustaining a hip fracture as well as the 10-year probability of having a major osteoporotic fracture, defined as clinical spine, forearm, hip, or shoulder fracture (Unnanuntana et al 2010).

In the current practice, when an elderly patient presents with a fracture following trivial trauma, osteoporosis is a presumptive diagnosis after excluding secondary causes of bone loss. A baseline bone mineral density measurement is advised for these patients. In the absence of fracture, the gold standard of diagnosis of primary osteoporosis in asymptomatic patients remains the measurement of bone mineral density using DXA (Clayer and Bauze 1989). The BMD measurement gives an accurate reflection of bone mass. The risk of fracture is increased 2 folds for each SD reduction in BMD.

Most studies of fracture of the proximal femur claim that generalized osteoporosis is the major etiological factor, although none has established a densitometric fracture threshold above which such fractures would not occur. Dual energy x-ray absorptiometry techniques have been validated for the quantitative assessment of bone mass at two skeletal sites particularly at risk of osteoporotic fracture, i.e., lumbar spine and proximal femur. These measurements assess areal bone mineral density (BMD), which integrates the size of the bone and its thickness, as well as the true volumetric density. Areal bone density provides useful information

relative to fracture risk, since there is an inverse relationship between incidence of osteoporotic fractures and area of BMD.

Several studies have concluded that incidences of osteoporosis and osteoporosis-related fractures (hip, spine, distal radius, and humerus) vary across the world. It is reasonable to hypothesize that Malaysia might be a low-risk country for osteoporosis because it is an Asian country. However, there is a lack of studies and insufficient information to confirm this theory. In addition, comparison rates with other countries have not yet been established (Lee et al 2013).

Furthermore, the role of osteoporosis in the occurrence of hip fractures remains controversial. Some investigators have found that patients with hip fractures have substantially less bone at various sites than subjects of similar ages who have not had fractures. Other investigators have found no significant difference in bone mass between these two groups (Bohr and schaad 1963).

Preventing osteoporosis would appear to be a logical way of preventing proximal femur fracture, but before embarking on such a program it would be essential to know the proportion of patients who would not have sustained a fracture had their bone mass been normal in our population. We therefore report a 12 month cross sectional study conducted in the Hospital Raja Perempuan Zainab II in Kelantan, aimed at obtaining an estimate of the proportion of proximal femoral fractures that are not related to generalized osteoporosis. Hospital Raja Perempuan Zainab II is one of the referral centers in managing osteoporosis and fracture related osteoporosis in the state of Kelantan.

1.1 Rationale of the study

1. Most of the previous studies were done in other countries. There was no previous study investigating the bone mineral density in fracture proximal femur particularly in elderly people in our population. Therefore the aim was to conduct a local study, specific to population in Kelantan.
2. The ever increasing incidence of fracture of the proximal femur is generating escalating costs. By knowing the true etiology of the fracture behind, we may provide the true preventive measures, hence managing the cost appropriately.

1.2 Research Questions

1. Do the elderly patient with fracture at the proximal femur, have bones which are really osteoporotic by WHO definition ?
2. Is the quantitative bone mineral density (T-score) of those with fracture proximal femur worse or similar with the WHO classification?

LITERATURE REVIEW

2. LITERATURE REVIEW

2.1 Introduction

Osteoporosis, characterized by generalized reduction in bone mass and strength that results in fragility fracture, has existed throughout human history. It was first noted in the 19th century by an English Surgeon, Sir Astley Cooper. He described osteoporosis as "the lightness and softness of bone that is acquired in the more advanced stages of life" and that "this state of bone favors much the production of fracture" (Raisz 2005).

In 1940, Fuller Albright (American physician and endocrinologist) described postmenopausal osteoporosis and suggest its correlation with estrogen deficiency. Subsequently, the concept of two forms of osteoporosis, postmenopausal with correlation to estrogen deficiency and senile type which is related to calcium deficiency and aging of the skeleton was proposed. This is later replaced by the current concept that osteoporosis is resulting from multiple pathogenetic mechanisms leading to loss of bone mass and microarchitectural deterioration of skeletal structure (Raisz 2005).

2.2 Definition osteoporosis

According to NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy (JAMA 2001), osteoporosis is defined as a systemic skeletal disorder characterized by compromised bone strength predisposing a person to an increased risk of fracture. Bone strength is determined by both bone density and bone quality. Bone density (g/cm² or g/cm³) is determined by peak bone mass and amount of bone loss.

$$BMD = \frac{\text{Bone Density (grams)}}{\text{Area (cm}^2\text{)}}$$

Bone quality refers to architecture, turnover, damage accumulation such as microfracture, and mineralization. A fracture occurs when a force that causes failure is applied to the osteoporotic bone. Thus, osteoporosis is a significant risk factor for fracture.

In women, the diagnosis of osteoporosis is made on the basis of bone mineral density (Table 2.1) as published in the WHO technical report series 843 (Organization 1994). The peak bone mineral density is achieved during the third decade of life and decline afterwards with advancing age (Figure 2.1). In women, this decline accelerates with menopause. The BMD value of -2.5 below the mean for the young adult (T score) identifies up to 95% of women at highest risk of fracture (Ryan 1997).

Table 2.1: The World Health Organization (WHO) working group classification of osteoporosis

Type	Bone Mineral Density (BMD) value
Normal	BMD within 1 SD of young adult reference range (T score > -1)
Osteopenia	BMD more than 1 SD but less than 2.5 SD below the young adult mean (T score between -1 and -2.5)
Osteoporosis	BMD value of 2.5 SD or more below the young adult mean (T score < -2.5)
Severe/ Established Osteoporosis	BMD value of 2.5 SD or more below the young adult mean with the presence of 1 or more fragility fractures
* T score comparison with young adult mean	

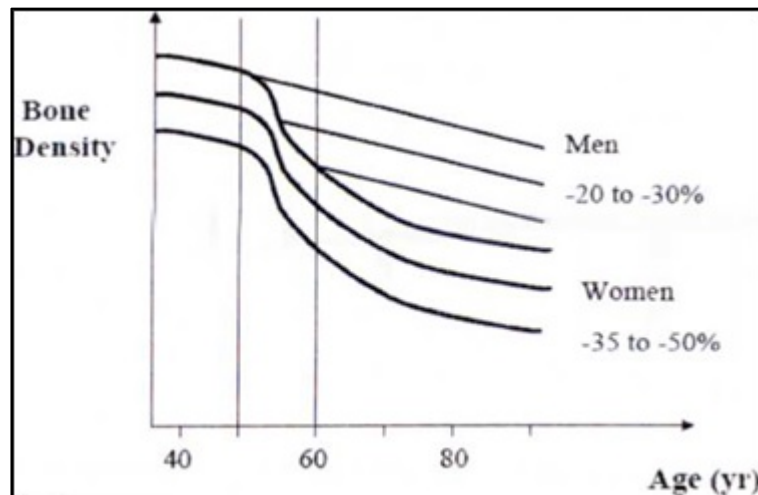


Figure 2.1: Bone Loss during adult life (Riggs and Melton III 1986)

2.3 Classification and clinical presentation of osteoporosis

Osteoporosis is often divided into primary and secondary osteoporosis syndrome (Riggs et al 2001). The basis of the classification is on whether or not the patient has a recognizable disease or due to other causes such as consumption of drugs resulting in bone loss (Table 2.2).

Table 2.2: Secondary Osteoporosis

Causes	Examples
Endocrine	<ul style="list-style-type: none"> • Cushing's syndrome • Hypogonadism • Thyrotoxicosis • Hyperparathyroidism
Drugs	<ul style="list-style-type: none"> • Glucocorticoids • Heparin • Anticonvulsants (phenytoin) • Immunosuppresants
Chronic diseases	<ul style="list-style-type: none"> • Renal impairment • Liver cirrhosis • Malabsorption/ post-gastrectomy • Chronic inflammatory polyarthropathies (e.g. rheumatoid arthritis)
Others	<ul style="list-style-type: none"> • Nutritional • Multiple myeloma and malignancy • Osteogenesis imperfecta

Three subgroups of osteoporosis fall under primary osteoporosis:

1. Type I osteoporosis (Postmenopausal)
2. Type 2 osteoporosis (Age related/Senile)
3. Idiopathic osteoporosis.

It is generally accepted that idiopathic osteoporosis that occur in young adults and involving both genders should be considered as a separate entity (Riggs et al 2001). The term involutional osteoporosis was previously used for type I and type 2 osteoporosis because both of the conditions occur in both genders and are strongly related to age. The sub classification of involutional osteoporosis into these two types was proposed by Riggs and Melton in 1986 and subsequently in other publications. Type 1 and 2 osteoporosis differed with respect to changes in regional bone mineral density, fracture pattern, associated hormonal changes and underlying pathophysiology (Riggs et al 2001).

Type 1 osteoporosis usually affects women within 15 to 20 years after menopause. The typical presentations are fractures occurring at sites that contain larger amounts of cancellous bone as in the vertebral body, distal end of radius and ankle. The vertebral fractures are typically of compression or collapse type and associated with reduction of more than 25% of vertebral height. These types of fractures are commonly painful and take longer time to subside (Riggs BL et al 2001.)

Type 2 osteoporosis affects both genders but it is twice as common in women as in men. It is a predominant form of osteoporosis in elderly over the age of 70 years old. The fracture pattern in this group is one that typically occurs at sites that contain both cancellous and cortical bone. The most common sites are the hip region and proximal humerus. In spine, typical features are of gradual and progressive deformity leading to dorsal kyphosis (the "dowager's hump"). These fractures are usually painless or associated with minimal pain. The radiographs show less than 25% vertebral height reduction with anterior wedge deformities. They mainly involved the mid thoracic area and occurred in multiple adjacent vertebrae. (Riggs et al 2001).

Table 2.3: Characteristics of osteoporosis type 1 and type 2 (Riggs et al 2001)

Characteristics	Type 1	Type 2
Age (years)	51-75	>70
Sex ratio (F:M)	6:01	2:01
Type of bone loss	Trabecular	Trabecular and cortical
Rate of bone loss	Accelerated	Not accelerated
Major fracture sites	Vertebrae (crush) and distal radius	Vertebrae (multiple wedge) and hip
Parathyroid function	Decreased	Increased
Estrogen effects	Mainly skeletal	Mainly extraskeletal
Main causes	Menopause plus individual predisposing	Factors related to aging including late effects of estrogen deficiency

The manifestations of osteoporosis type 1 and type 2 are closely related to underlying patterns of age related bone loss. Based on cross-sectional and longitudinal bone densitometric studies (Riggs et al 2001), there are two phases of age related bone loss identified. The slow age related or involutional loss and the accelerated phase that occur only in postmenopausal women due to the reduction of estrogen level.

The slow phase begins at about 35 - 40 years old and continues throughout life. The rate of loss is less than 0.5% per year and similar in both gender and results in loss of similar amount of cortical and cancellous bone. It includes for maximum bone loss of 20% in total. It is due to subtle uncoupling of rate of bone formation and resorption. The accelerated phase occurs only in postmenopausal women. It superimposes the slow loss and results in loss of more cancellous bone.

The most affected sites are the spine and distal end of radius. The accelerated loss last about 10 years with the rate of approximately 1 % to 2% per year and maximum total loss of 10% throughout. The main loss usually occur during the first three years of menopause.

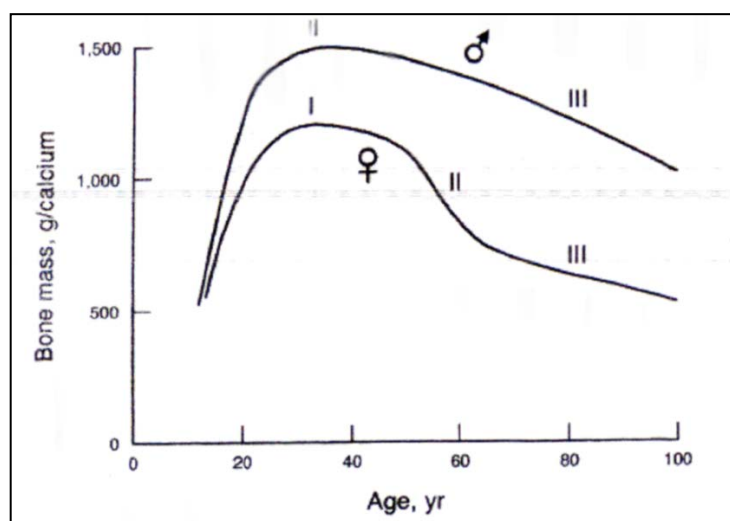


Figure 2.2: Changes in bone mass in aging men and women showing pattern of bone loss. (I) Peak bone mass, (II) rapid phase of bone loss in women around menopause, (III) is age related bone loss, similar in men and women (Riggs et al 2001).

Of all osteoporotic related fractures, fractures around the hips are the most disabling. It is associated with higher morbidity and mortality of up to 20% within the first year of injury. Majorities are disabled and only 25% resume premorbid activities (Jensen and Bagger 1982). It imposes a considerable financial burden on the health services due to related problem of patient's immobilization and cost of hospitalization. In the European Union, osteoporosis patients occupied 500,000 hospital bed-nights per year, and this was expected to double by 2050 worldwide (Clayer and Bauze 1989).

Few studies regarding the incidence of hip fracture have been reported in Asian countries. The Asian Osteoporosis Study was the first multicenter study documenting and comparing the incidence of hip fracture in four Asian countries namely the Hong Kong SAR, Singapore, Malaysia and Thailand (Chiang Mai) in 1997. In Hong Kong the age-adjusted rates for hip fracture in men and women were 180 and 459 per 100,000 respectively, 88 and 218 per 100,000 in Thailand, 164 and 442 per 100,000 in Singapore. In Malaysia, the incidence was 88 and 218 per 100,000 populations. The study showed moderate variation of incidence hip fracture among Asian countries and the rates were highest in urbanized countries (Lau et al 2001).

2.4 Risk factor for osteoporosis

Osteoporosis is a silent systemic disease without any obvious symptoms until the event of fragility fracture. Since population screening is not cost effective, identification of individual at risk will help in case finding (Eddy et al 1998). The major factors contributing to increased risk of osteoporosis and osteoporotic fracture

in post menopausal women are shown in Table 2.4 (National Osteoporosis Foundation 1999).

L. Koh identified the combination weight and age as the most reliable risk factors to predict osteoporosis in post-menopausal Asian women (Koh et al 2001). Postmenopausal women were stratified into low, medium and high risk group based on their weight and height. Validation studies were performed in four Asian countries (Japan, Korea, Singapore and China) followed by design of a simple chart known as Osteoporosis Self-Assessment tool for Asians (Figure 2.3). The validation studies found that, those who belong in the high risk group are at 61% risk of having osteoporosis (Table 2.5). The high risk group patients are recommended for BMD measurement, however pharmacologic treatment should be considered in this group even if BMD is not available. This chart was used as screening tool to target BMD measurement to high risk women and reduced the overall need of BMD measurements.

Table 2.4: Risk Factors (From National Osteoporosis Foundation 1999: Physician's guide to prevention and treatment of Osteoporosis)

Type	Risk Factor
Non--modifiable	<ul style="list-style-type: none"> • Advancing age • Ethnic group • Female gender • Premature menopause (< 45 years) including surgical menopause • Slender build • Family history of • Osteoporosis in first degree relative • Personal history of fracture as an adult
Modifiable	<ul style="list-style-type: none"> • Low calcium intake • Sedentary lifestyle • Smoking cigarette • Excessive alcohol intake • Excessive caffeine intake • Low body weight (<127lb) • Estrogen deficiency • Impaired vision • Recurrent falls

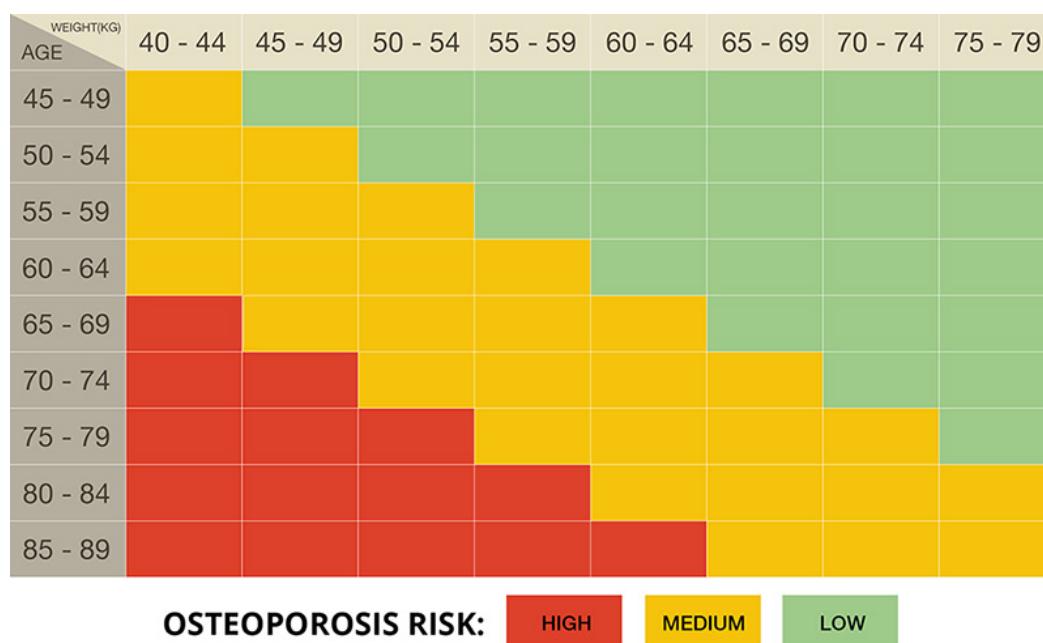


Figure 2.3: Osteoporosis Self-assessment Tool for Asia (OSTA) and treatments

Table 2.5: Risk stratification

Risk Level	% with osteoporosis	Recommended Approach
Low	3	BMD measurement probably not necessary unless other risk factors are
Medium	15	Measure BMD and consider pharmacologic treatment if BMD is low
High	61	BMD measurement if possible. Consider pharmacologic treatment even if BMD is not available.

2.5 Diagnosis

A thorough clinical evaluation which includes a detailed history, physical examination and appropriate laboratory investigations to rule out secondary causes of osteoporosis as mentioned before, are the first key step to diagnose primary osteoporosis. Multiple risk factor assessment does not predict bone mass precisely (Slemenda et al 1990), but it is the mainstay in decision making to identify patients who are at risk and require further investigation.

Those who presented with fragility fracture following trivial trauma, the diagnosis of osteoporosis is presumed after secondary causes are ruled out. BMD measurement is recommended in these patients. However, pharmacological treatment is still initiated even if BMD is not available. Those without fractures, BMD measurement is still the gold standard to diagnose osteoporosis.

Three aims of investigation are:

1. To confirm the diagnosis of osteoporosis.
2. To assess fracture risk.
3. To exclude secondary causes.

There is no single specific laboratory investigation available to diagnose primary osteoporosis. The role of Full blood count and ESR (Erythrocyte Sedimentation Rate) are to assess general condition of the patient and to rule out 'red flags' such as infection and malignancy. In other metabolic causes causing bone

fragility such as rickets and osteomalacia, serum calcium and phosphate will be show abnormality. Alkaline phosphatase is a marker for bone turnover. Elevated level is expected in fractures or primary or secondary malignancies of the bone. Renal function test is done in those suspected of osteoporosis secondary to chronic or end stage renal failure. Other specific laboratory investigation should be performed to rule out secondary causes of osteoporosis based on clinical suspicion which include:

1. Thyroid function test for assessment of hyper or hypothyroidism.
2. Testosterone level for assessment of hypogonadism in male.
3. Follicular stimulating hormone and luteinizing hormone level for confirmation of menopause and identifying the cause of estrogen deficiency.
4. Urine Bence Jones and serum electrophoresis performed in suspicion of multiple myeloma.

Currently, there is no consensus as to the most cost-effective, sensitive testing panel for secondary causes of osteoporosis. Testing should be based on the individual, with an eye to postmenopausal women with risk factors for secondary osteoporosis, and any man or premenopausal woman with history of fragility fracture or unexplained bone loss (Kelman and Lane 2005).

2.5.1 Specific Investigation

The role of plain radiograph

Osteoporosis will only be apparent in plain radiograph only after more than 30% of bone loss has occurred. Therefore, early diagnosis of osteoporosis is not possible using this method. Before the introduction and development BMD measurement using DXA scan, several plain radiographic methods have been developed for the diagnosis of osteoporosis. These methods involved the study of changes of bone morphology in plain radiographs including the spine and the proximal femur and the metacarpal bones (Exton-Smith et al 1969).

In 1960, Barnett and Nordin firstly introduced the use of cortical thickness as a predictor of skeletal mineralization. Afterwards, cortical measurements were used extensively to estimate osteoporotic changes in the bone. The metacarpal index (MCI) is combined cortical thickness of both sides, divided by the outer diameter of the measuring site, the mid shaft of the second metacarpal. MCI is reduced with age especially in postmenopausal women and correlates with axial bone mass in group studies. It can be used for diagnosis of osteoporosis and also for monitoring changes. The test is inexpensive and fast. Currently MCI is regaining its popularity among tests for bone strength and quantification of bone mass (Nielsen 2001). However, this test is not a potent predictor for osteoporotic fracture when studied over a long period of time (Kiel et al 2001).

Concerning on anatomy, the proximal femur is a choice site for the plain radiographic study of osteoporosis. Osteoporosis affect different areas of the skeleton in different proportions but the spine and the proximal femur are the main sites of the main symptoms of the disease such as vertebrae compression fracture and neck of femur fractures which make them the most relevant sites for study. However, since

the spinal radiographs are difficult to interpret, the proximal femur becomes the area of choice. Bone mineral density measurement using DXA scan was later developed and accepted as the gold standard method for diagnosis of osteoporosis. It is not a suitable for population screening purposes due of constraints of cost and availability. Quantitative measurement of bone is not possible with plain X-rays but attempts have been made to correlate the bone quality assessed by index measurements using plain radiographs with the bone mineral density as measured with DXA scan.

Singh developed the index measurement of hip region based on changes in distribution of the trabecular pattern in the femoral neck in patients with osteoporosis (Figure 2.4/Table 2.6). He studied the plain radiographs of non fractured hips of 35 patients presented with osteoporotic hip fracture and comparing them with the histological changes of the bone taken from the iliac crest. They found a highly positive correlation between these two (Singh et al 1970). The Singh Index was developed based on this finding. Based on the finding with increasing degrees of bone loss, six different trabecular patterns can be recognized in the upper femur. He suggested that these patterns can be utilized as radiographic scale for the diagnosis and grading of osteoporosis.

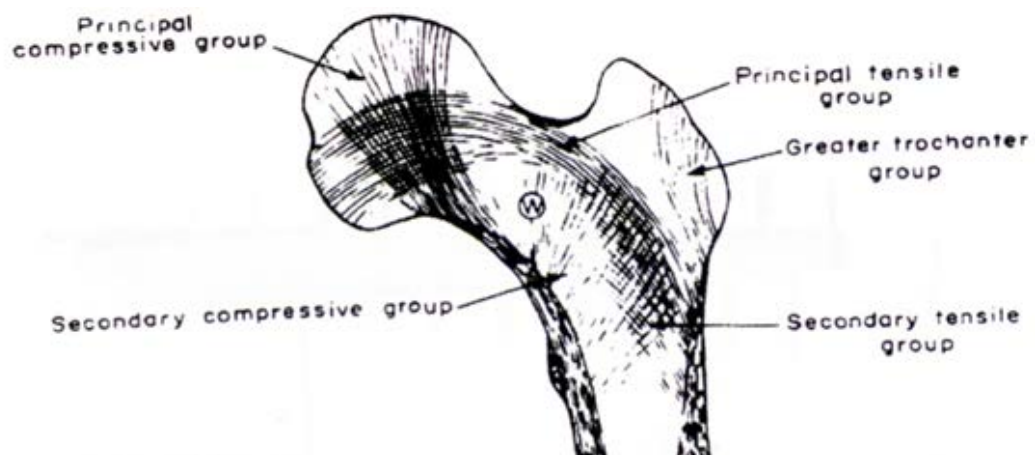


Figure 2.4: Normal trabecular pattern of proximal femur (taken from Manmohan Singh et al 1970)

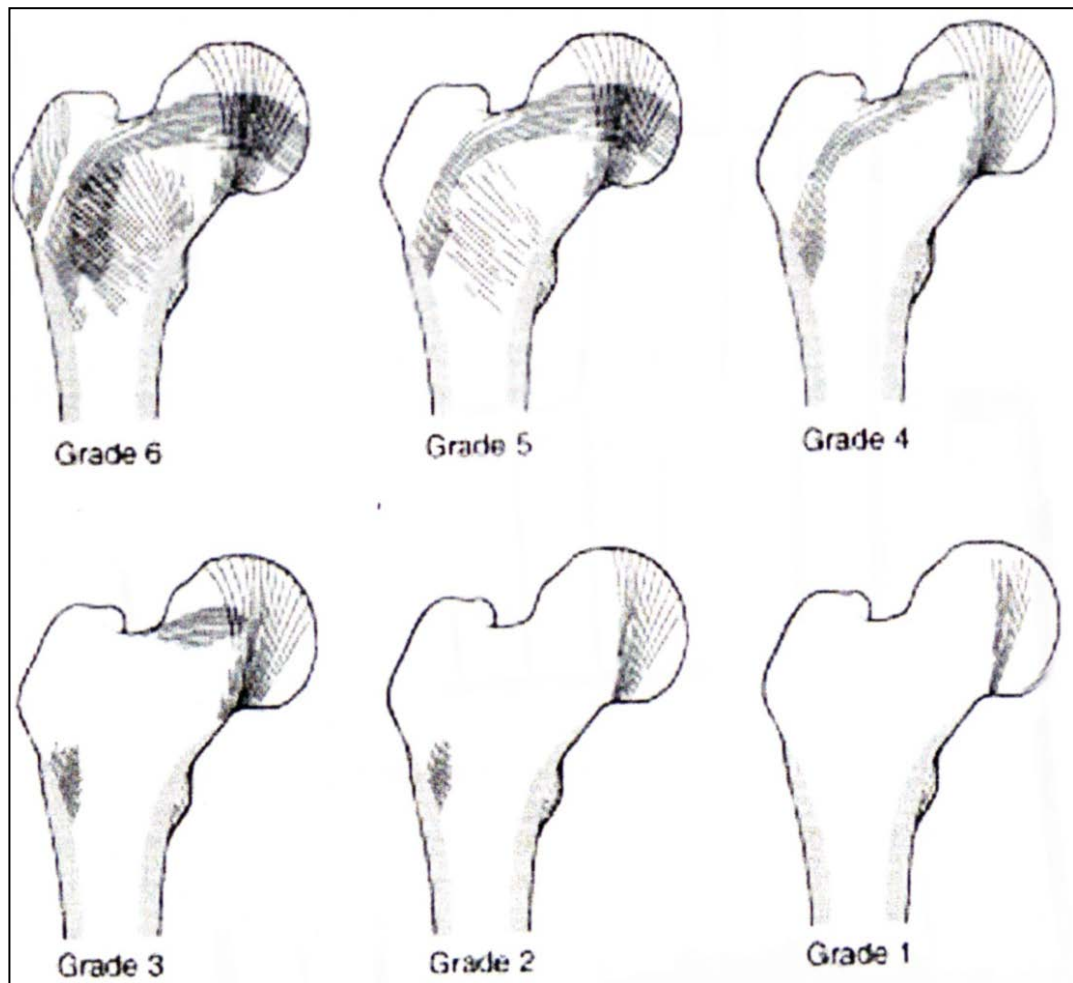


Figure 2.5: Singh Index (Graphics are from orthoedicnotes.blogspot.com)

Table 2.6: Singh index description (from Manmohan Singh et al 1970)

Grades	Description
Grade 1	Principle compressive trabeculae are markedly reduced in number and are no longer prominent.
Grade 2	Only the principle compressive trabeculae stand out prominently, remaining trabeculae have been essentially absorbed
Grade 3	There is a break in the continuity of the principal tensile trabeculae opposite the greater trochanter, this grade indicates definite osteoporosis
Grade 4	Principle tensile trabeculae are markedly reduced in number but can still be traced from the lateral cortex to the upper part of the femoral neck (Borderline)
Grade 5	Principle tensile and principle compressive trabeculae is accentuated. Ward's triangle appears prominent (early bone loss)
Grade 6	All the normal trabecular groups are visible and upper end of the femur seems completely occupied by cancellous bone (normal young individual)

T Masud et al 1995, in the Chingford Study analyzing the screening potential of Singh Index found good intra observer reproducibility and significant correlation with BMD. Using the criteria of "osteoporosis < Singh grade 4" the sensitivity and specificity of Singh Index method in diagnosing low bone mass was 35.1% and 90.0%, respectively. However, large intra observer variations and low reliability of the method were found in many other subsequent studies. This method is no longer popular especially for quantification of osteoporosis (Koot et al 1996, Hauschild et al 2009, Soontrapa et al 2005, Salamat et al 2010). Koot et al 1996 found no significant correlation between BMD and Singh Index. Due to its subjective character, its predictive value for the mechanical quality of bone in individual patients remains uncertain. However, in some cases it can be used to replace the measurement of BMD especially in cases of markedly reduced bone mineral density (Krischak et al 1999).

The role of BMD measurement

Judging bone density by visual observation and interpretation of a radiograph can be imprecise because technical considerations, such as patient size, exposure, and processing factors, influence how dense the bones appear. Bone densitometry, by contrast, calculates BMD in numerical units and thus provides a more accurate representation of bone mineral losses (Adams et al 2008).

Bone mineral density measurements have an important role in the evaluation of patients at risk of osteoporosis, diagnosis and in the appropriate use of anti fracture treatment. The WHO committee on osteoporosis defined osteoporosis based on the bone density. Based on the standard total BMD of the hip, normal bone is

defined as BMD measurement greater than $833\text{mg}/\text{cm}^2$, osteopenia is when BMD between 833 and $648\text{mg}/\text{cm}^2$ and osteoporosis when BMD is lower than $648\text{mg}/\text{cm}^2$. Severe osteoporosis is when there has been fragility fracture.

In 1963, single-photon absorptiometry (SPA) was introduced. This device could quantitatively measure the BMD of the peripheral bones (Cameron and Sorenson 1963). The energy level used was sufficient for the BMD measurement of appendicular bones but not for that of central skeletal sites.¹⁵ Dual-photon absorptiometry (DPA) was then developed (WAHNER et al 1988). Both SPA and DPA used radionuclide sources that decayed and required regular replacement. With the slow scanning, there occurred undesirable incidents, such as the patients moving during the scan, rendering poor quality of the image and limiting reproducibility. In the mid-1980s, DXA was developed. Unlike the 2 previous devices, DXA used low-energy x-ray beam with high photon flux that permitted faster scanning.

Currently available methods for measuring bone mineral density in our country include:

1. Dual energy X-ray absorptiometry (DXA)
2. Quantitative computed tomography (QCT)
3. Single energy X-ray absorptiometry (SXA)

In most centers the best method for BMD measurement is central DXA scan.

Three major roles are:

1. Diagnosis of osteoporosis
2. Assessment of patient's risk of fracture
3. Monitoring response of treatment

The advantages of using central DXA scan include:

1. The hip BMD is the most reliable measurement for prediction of hip fracture risk and the predictive value is similar both in men and women (Johnell et al 2005).
2. The use of spine BMD for monitoring treatment.
3. The consensus that in post menopausal women and older men the spine and hip DXA scan should be interpreted using WHO t-score definition of osteoporosis.
4. Short scan time, easy patient set up for scanning, low radiation dose , stable calibration, availability of reliable reference range and good measurement precision.

DXA scanners evaluate bone mineral density by measuring the transmission of X-rays through the body at two different photon energies. The X-ray transmission through any physical object can be decomposed into the equivalent areal densities (g/cm^2) of any two chosen reference material. The two materials for DXA scan are bone mineral and the soft tissue. Provided that the object under study composed solely of the two reference material, the computed areal densities will accurately reflect the densities. There are limitations of this method. The scan is a two dimensional (2D) projection image, the measurement of areal densities are affected by bone size and the true 3D volumetric density of the bone. This problem causes the difficulty with the interpretation of paediatric DXA. It may affect adults reading to certain extent as well causing difference between gender and ethnic group and also less obvious effect due different bone sizes in different individuals.

Central DXA scan involve examination of the hip and spine. The results are presented as T-score and Z-score (Figure 2.6). The T-score are calculated by taking the difference between patient's measured BMD and the mean BMD of young adults matched for gender and ethnic group and expressing the difference relative to the young adult population standard deviation. It is used to diagnose the severity of osteoporosis.

$$T\ score = \frac{\text{Measured BMD} - \text{Mean BMD of young adult}}{\text{Standard Deviation of young adult population}}$$

The hip and spine DXA scan results in postmenopausal women and adults more than 50 years are interpreted using T-score according to the WHO definition of osteoporosis (Table 2.1).

The Z-score is calculated by taking the difference between patients measured BMD and healthy subjects matched for age, gender and ethnic group.

$$Z\ score = \frac{\text{Measured BMD} - \text{Age matched mean BMD}}{\text{Standard Deviation of age matched population}}$$

The Z-score is used to identify patients who are at risk for fracture. The evaluation of fracture risk is determined by prospective studies of incident of fractures. When patients are divided into quartile on the basis of their BMD, an inverse relationship is found between fracture incidence and BMD. To describe this relationship, the data are fitted with a gradient- of-risk model in which the fracture probability increases exponentially with decreasing Z score with gradient. Results are usually expressed in terms of the relative risk (RR), which is defined as the increased risk of fracture for each unit decrease in Z score.